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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/086,133	02/28/2002	Sridhar Krishna Rabindran	ACY-33,316-D2	3539

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WYETH
PATENT LAW GROUP
FIVE GIRALDA FARMS
MADISON, NJ 07940

EXAMINER
TRAVERS, RUSSELL S

ART UNIT	PAPER NUMBER
1617	4

DATE MAILED: 06/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/086,133	Rabindran et al
Examiner	**Art Unit**
R.S. Travers J.D., Ph.D.	1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1 and 7* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1 and 7* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

The amendment filed February 26, 2002, and Information disclosure statement filed November 21, 2002 have been received and entered into the file.

Claims 1 and 7 are presented for examination.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to make and/or use the invention, and thereby failing to provide an enabling disclosure.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to set forth criteria allowing the skilled practitioner to identify those "chemosensitizing compounds that reverse non P-gp/non MRP multiple drug resistance in cancer cells exhibiting non P-gp/non MRP drug resistance phenotype", "chemosensitizing compounds that reverse BCRP-mediated multiple drug resistance in cancer cells", "test compound(s)", or chemotherapeutic agents required to practice the claimed invention. Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. In the instant case, only a limited number of compounds useful as "chemosensitizing compounds that reverse non P-gp/non MRP multiple drug resistance in cancer cells exhibiting non P-gp/non MRP drug resistance phenotype", "chemosensitizing compounds that reverse BCRP-mediated multiple drug resistance in cancer cells", "test compound(s)", or chemotherapeutic agent examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological

activity. The instant claims read on all "chemosensitizing compounds that reverse non P-gp/non MRP multiple drug resistance in cancer cells exhibiting non P-gp/non MRP drug resistance phenotype", "chemosensitizing compounds that reverse BCRP-mediated multiple drug resistance in cancer cells", any "test compound", or any chemotherapeutic agent, necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Simply stated, the instant claims are an invitation to experiment for solutions to resistance experienced with chemotherapeutic regimens. The skilled artisan would respond to chemo-therapeutic failures by employing alternative drugs, or instituting concomitant administration of old and well known chemotherapeutic agents as taught by the Merck Manual. As herein claimed, and disclosed, the envisioned invention appears to be "a mere wish or plan for obtaining the claimed chemical invention" admonished by the Court of Appals for the Federal Circuit in *Regents of the University of California v. Eli Lily & Co.* , (119 F3d 1559, 1566; USPQ2d 1398, 1406, (CAFC 1997), *cert denied,* 523 U.S. 089, 118 S.Ct. 1548 (1998)). To capture this subject matter Applicants are required to provide "a precise definition , such as by structure, formula, chemical name, or physical properties" of those compounds envisioned ((*Regents of the University of California v. Eli Lily & Co.*, *supra,* at 1566). Absent such

information the instant claims fail to meet the enablement requirement set forth under 35 USC 112.

Claims 1 and 7 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 1 and 7 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 7 are rendered indefinite by the phrases "chemosensitizing compounds that reverse non P-gp/non MRP multiple drug resistance in cancer cells exhibiting non P-gp/non MRP drug resistance phenotype", "chemosensitizing compounds that reverse BCRP-mediated multiple drug resistance in cancer cells" and "test compound", and thereby failing to clearly set forth the metes and bounds of the patent protection desired. Criteria defining medicaments that are "chemosensitizing compounds that reverse non P-gp/non MRP multiple drug resistance in cancer cells exhibiting non P-gp/non MRP drug resistance phenotype", "chemosensitizing compounds that reverse BCRP-mediated multiple drug resistance in cancer cells" or a "test compound" are not set forth in the specification, thereby failing to provide information defining the instant inventions metes and bounds. Applicant's terms fail to

clearly define the subject matter encompassed by the instant claims, thus are properly rejected under 35 USC 112, second paragraph.

Claims 1 and 7 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 7 are rendered indefinite by the phrases "chemosensitizing compounds that reverse non P-gp/non MRP multiple drug resistance in cancer cells exhibiting non P-gp/non MRP drug resistance phenotype", those "chemosensitizing compounds that reverse BCRP-mediated multiple drug resistance in cancer cells", a "test compound" and thereby failing to clearly set forth the subject matter of the patent protection desired. Examples of what "chemosensitizing compounds that reverse non P-gp/non MRP multiple drug resistance in cancer cells exhibiting non P-gp/non MRP drug resistance phenotype", those "chemosensitizing compounds that reverse BCRP-mediated multiple drug resistance in cancer cells", or those compounds effective as a "test compound" are not set forth in the specification. This failure additionally obscures any relationship between these compounds possibly envisioned for the instant invention. No clear relationship exists between "chemosensitizing compounds that reverse non P-gp/non MRP multiple drug resistance in cancer cells exhibiting non P-gp/non MRP drug resistance phenotype", "chemosensitizing compounds that reverse

BCRP-mediated multiple drug resistance in cancer cells", or "test compound(s)" recited in the instant claims. Absent exemplification, the skilled artisan could not establish the identity of compounds that could be envisioned as "chemosensitizing compounds that reverse non P-gp/non MRP multiple drug resistance in cancer cells exhibiting non P-gp/non MRP drug resistance phenotype", "chemosensitizing compounds that reverse BCRP-mediated multiple drug resistance in cancer cells", or "test compound(s)". Applicant's phrases fail to clearly define the subject matter encompassed by the instant claims, thus is properly rejected under 35 USC 112, second paragraph.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 1 and 7 are rejected under 35 U.S.C. § 103 as being unpatentable over Cui et al, Naito et al in view of the Merck Manual.

Cui et al and Naito et al teach the various compounds, to include those herein claimed as old and well known in combination with various pharmaceutical carriers and excipients in a dosage form. These medicament is taught as useful for treating neoplastic diseases, viewed by the skilled artisan as indistinguishable from those uses herein claimed. Naito et al teach resistance mediated by factors other than P-gp/MRP drug resistance phenotype. Attention is directed to Naito et al teaching over expression of the mRNA for this protein, yet no over expression of the protein, as herein envisioned. Examiner cited teachings disclosed the envisioned compounds, the resistance mechanisms herein envisioned, and those methods employed to ascertain resistance, rendering obvious those factors disclosed as a basis for the instant invention. Claims 1 and 7, and the primary references, differ as to:

1) the concomitant employment of these medicaments, and

2) employing compounds concomitantly to provide therapy for resistant neoplasms. .

It is generally considered prima facie obvious to combine compounds each of which is taught by the prior art to be useful for the same purpose, in order to form a composition which is to be used for the very same purpose. The idea for combining them flows logically from their having been used individually in the prior art. As shown by the recited teachings, the instant claims define nothing more than the concomitant use of conventional anti-neoplastic agents. It would follow that the recited claims define

prima facie obvious subject matter. Cf. In re Kerhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980).

Claims 1 and 7 specifically require the addition of compounds concomitantly to neoplasms coupled with a determination of therapeutic effectiveness. Merck Manual teaches the treatment of neoplastic diseases as highly individual, with measures anti-neoplastic effectiveness as the goal of therapeutic success. Possessing Examiner's teachings the skilled artisan would be motivated to employ the claimed compounds concomitantly and measure anti-neoplastic effectiveness. The skilled artisan would have seen administering the disclosed compounds concomitantly to overcome resistance as residing in the skilled artisan purview.

No claims are allowed.

Any inquiry concerning this communication should be directed to Russell Travers at telephone number (703) 308-4603.

Russell Travers J.D., Ph.D.
Primary Examiner
Art Unit 1617